

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

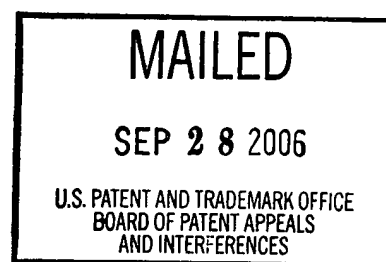
UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte ALESSANDRA D'AZZO and ERIK JACOBUS BONTEN

Appeal No. 2005-2739
Application No. 09/966,893

ON BRIEF



Before SCHEINER, MILLS and GRIMES, Administrative Patent Judges.

SCHEINER, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims to a pharmaceutical composition comprising a protein useful for treating a lysosomal storage disorder, other than Fabry disease, wherein the protein has been produced in an insect cell culture. The examiner has rejected the claims as lacking enablement, as lacking adequate written descriptive support, and as anticipated by the prior art. We have jurisdiction under 35 U.S.C. § 134.

Background

"Lysosomal storage disorders (LSDs) are a group of genetically inherited disorders . . . characterized by a deficiency of one or more specific lysosomal enzymes which causes an accumulation of undigested material (macromolecules) inside the lysosome. This accumulation causes lysosomes to enlarge, leading eventually to cell

degeneration . . . [and] accumulation of macromolecules in various tissues and organs of the body causing these organs to function less efficiently, resulting in progressive deterioration . . . and eventually death.” Specification, page 2.

“A number of [lysosomal storage disorders] have been treated using enzyme replacement therapy and several clinical trials are ongoing in this area. For example, α -Galactosidase A has been used to treat Fabry disease and glucocerebrosidase has been used to treat Gaucher Disease” (id., page 6). Table 1 of the specification lists dozens of lysosomal storage disorders and their associated enzyme deficiencies, as well as supporting references.

“Insect cells . . . used for expression of foreign proteins, typically via infection with a recombinant baculovirus, accomplish most of the same post-translational modifications as mammalian cells, including phosphorylation, N- and O- linked glycosylation, acylation, disulphide cross-linking, and oligomeric assembly.” Id., page 2. “Production of foreign protein in insect cells is generally considered [to be] more cost effective and efficient . . . [than production in] mammalian cell[s]” (id., pages 1-2), but the differences in post-translational modifications between insect and mammalian cells are not well understood (id., page 2). According to appellants, “[t]hese differences and their ill-defined nature are generally considered a disadvantage of producing proteins in insect cells” (id.).

“The therapeutic activity of proteins . . . used to treat lysosomal storage disorders is attributed primarily to the lysosomal activity of such proteins in macrophages.” Id., page 9. “The present invention is based on the discovery that proteins produced in insect cells by standard baculovirus expression systems are glycosylated in a unique way which makes them susceptible to uptake by macrophages via mannose receptors

that are present on macrophage membranes but which are not normally present on the membranes of other cells” Id.

The Claims

Claims 8-13 are the subject of appeal. Claims 1-7 and 14-20 are also pending, but have been withdrawn from consideration. Claims 8-13 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement and adequate written descriptive support. In addition, claims 8-13 stand rejected under 35 U.S.C. § 102(a) as anticipated by Sharp. Claims 8-13 read as follows:

8. A pharmaceutical composition comprising a protein useful for treating a lysosomal storage disorder other than Fabry disease that is selectively imported into macrophages when administered to a subject and a pharmaceutically acceptable carrier, wherein said protein is produced in an insect cell culture.

9. The composition of claim 8 wherein said lysosomal storage disorder is Galactosialidosis.

10. The composition of claim 8 wherein said protein is protective protein/cathepsin A (PPCA).

11. The composition of claim 8 wherein said insect cell culture comprises cells derived from the species selected from the group consisting of *Spodoptera frugiperda* and *Tricoplusia ni*.

12. The composition of claim 11 wherein said cells are *Spodoptera frugiperda* Sf9 cells.

13. The composition of claim 8 wherein said protein is produced in the cell culture using a baculovirus expression system.

Discussion

Written Description

The examiner rejected claims 8-13 under 35 U.S.C. § 112, first paragraph, “as failing to comply with the written description requirement.” Examiner’s answer, page 3.

The examiner notes that the specification describes in vitro and in vivo experiments involving “baculovirus-expressed neuraminidase and baculovirus-expressed PPCA” (Examiner’s Answer, page 5), but argues that “the specification does not provide the specific amino acid sequence and structure of the . . . protein[s]” (id.). Moreover, the examiner argues that “[t]he specification fails to provide additional representative proteins useful for treating any lysosomal storage disorder” (id.), although the claims encompass “many proteins with widely differing structural, chemical, and physical characteristics” and “many widely differing lysosomal storage disorders that have widely differing etiologies based on their respective enzyme and/or protein deficiencies” (id., page 4).

We disagree with the examiner’s rationale and conclusion. “The ‘written description’ requirement serves a teaching function, . . . in which the public is given ‘meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time.’” University of Rochester v. G.D. Searle & Co., Inc., 358 F.3d 916, 922, 69 USPQ2d 1886, 1891 (Fed. Cir. 2004) (citation omitted). Another “purpose of the ‘written description’ requirement is . . . [to] convey with reasonable clarity to those skilled in the art that, as of the filing date [], [the applicant] was in possession of the invention.” Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). See also Enzo Biochem Inc. v. Gen-Probe Inc., 296 F.3d 1316, 1329, 63 USPQ2d 1609, 1617 (Fed. Cir. 2002). The requirement is satisfied when the specification “set[s] forth enough detail to allow a person of ordinary skill in the art to understand what is claimed and to recognize that the inventor invented what is claimed.” University of Rochester, 358 F.3d at 928, 69 USPQ2d at 1896. Whether or not a

specification satisfies the requirement is a question of fact, which must be resolved on a case-by case basis (Vas-Cath, 935 F.2d at 1562-63, 19 USPQ2d at 1116), and it is the examiner's "initial burden [to] present[] evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims" (In re Wertheim, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976)).

"Applicants have some flexibility in the 'mode selected for compliance' with the written description requirement" (University of Rochester, 358 F.3d at 928, 69 USPQ2d at 1896), and it is well settled that actual reduction to practice is not necessary to satisfy the requirement (id. at 926, 69 USPQ2d at 1894). Finally, the court has made it clear that other factors, including the level of skill in the art, are relevant to whether a description satisfies § 112. See Capon v. Eshhar, 418 F.3d 1349, 1358-59, 76 USPQ2d 1078, 1085 (Fed. Cir. 2005) ("[T]he determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter.").

Appellants point out that the claims "encompass only those proteins useful for treating lysosomal storage disorders [] other than Fabry disease" and "[a] comprehensive list of such proteins is provided in Table 1 of the specification" (Appeal Brief, page 7), together with "references to scientific literature and/or Genbank accession numbers disclosing the structure (amino acid sequence) of these proteins" (id., page 5). Appellants argue that "[t]his structural information can be used to create nucleic acid vectors for the expression of these proteins in any desired cell type, including insect

cells” (*id.*, pages 5-6), “since this process, like the protein component of the invention, was also well known in the art” (*id.*, page 6).

The examiner has not explained why these teachings would not have conveyed with reasonable clarity to one of skill in the art that appellants were in possession of a genus of enzymes implicated in a host of lysosomal storage disorders. The examiner’s conclusory assertion that the working examples are not representative of a larger genus is insufficient to meet the examiner’s “initial burden [to] present[] evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims” (*Wertheim*, 541 F.2d at 263, 191 USPQ at 97).

The rejection of claims 8-13 as lacking adequate written descriptive support under 35 U.S.C. § 112, first paragraph, is reversed.

Scope of Enablement

Claims 8-13 stand rejected under 35 U.S.C. § 112, first paragraph, “because the specification, while being enabling for [a] composition comprising a protective protein/cathepsin A (PPCA) protein useful for treating galactosialidosis, does not reasonably provide enablement for any other embodiment” (Examiner’s Answer, page 6).

“[A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.” *In re Marzocchi*, 439 F.2d 220, 2223, 169 USPQ 367, 369 (CCPA 1971) (emphasis original). “[I]t is incumbent upon the Patent Office . . . to explain why it

doubts the truth and accuracy of any statement in the supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.” Id. at 224, 169 USPQ at 370.

In a nutshell, the examiner argues that “[t]he amount of experimentation to search for any pharmaceutical composition comprising any polypeptide of any structure and function which can be used to treat any patient having any lysosomal storage disorder . . . without harming the patient is enormous and undue.” Examiner’s Answer, page 9. According to the examiner, “[s]uch experimentation entails determining whether a particular disease is a lysosomal storage disorder disease, determining the etiology of the disease, searching and screening for any protein of any structure and function, and determining whether any pharmaceutical composition comprising the protein would be useful in treating the patient having any lysosomal storage disorder without harming the patient.” Id., pages 9-10.

Nevertheless, we agree with appellants that the examiner has not established that practicing the full scope of the claims would have required undue experimentation. Appellants point out that “practice of the claims does not entail determining whether a particular disease is a lysosomal storage disorder and determining the etiology of the disease” as “[t]his information is known and is provided in Table 1” (Appeal Brief, page 10), wherein particular proteins “are clearly associated with the lysosomal storage disorder they can be used to treat” (id.). Moreover, appellants argue that “[m]any of the proteins encompassed within the claimed compositions, produced by a means other than insect cell production, have already been used or are being tested in clinical trials to treat lysosomal storage disorders.” Id., page 9. Finally, appellants argue that the examiner

“has not provided any basis for disputing the ability of the skilled artisan to produce the claimed pharmaceutical compositions . . . [or] to administer such compositions by conventional techniques.” Id.

We find that the examiner has not adequately explained why practicing the full scope of the claims would have required undue experimentation. Given the guidance and direction set forth in the specification, the process of making and using proteins with the properties required by the claims would appear to require nothing more than routine, iterative experimentation. In any case, it is well settled that “appellants are not required to disclose every species encompassed by their claims even in an unpredictable art.” In re Angstadt, 537 F.2d 498, 504, 190 USPQ 214, 218 (CCPA 1976).

The rejection of claims 8-13 under 35 U.S.C. § 112, first paragraph, for lack of enablement is reversed.

Anticipation

Turning to the rejection of claims 8-13 under 35 U.S.C. § 102(a), we find that the claimed subject matter is not identically described by Sharp.¹ As stated in In re Arkley, 455 F.2d 586, 587, 172 USPQ 524, 526 (CCPA 1972), an anticipatory reference under 35 U.S.C. § 102

. . . must clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound without any need for picking, choosing, and combining various disclosures not directly related to each other by the teachings of the cited reference. Such picking and choosing may be entirely proper in the making of a 103, obviousness rejection, where the applicant must be afforded an opportunity to rebut with objective evidence any inference of obviousness which may arise from the similarity of the subject matter which he claims to the prior art, but it has no place in the making of a 102, anticipation rejection.

¹ Sharp, International Application WO 00/39150, published July 6, 2000

Sharp discloses TANGO 176, “a family of proteins with homology to lysosomal protective protein cathepsin A (PPCA)” (Sharp, page 27). According to Sharp, TANGO 176 “nucleic acid molecules, proteins . . . and antibodies . . . can be used in one or more of the following methods: a) screening assays; b) detection assays . . . ; c) predictive medicine (e.g., diagnostic assays, prognostic assays, . . .); and d) methods of treatment (e.g., therapeutic and prophylactic)” (*id.*, page 76). Moreover, TANGO 176 proteins may be expressed “in prokaryotic (e.g., *E. coli*) or eukaryotic cells (e.g., insect cells (using baculovirus expression vectors), yeast cells or mammalian cells) . . . [or] transcribed and translated *in vitro*, for example using T7 promoter regulatory sequences and T7 polymerase” (*id.*, page 66).

According to the examiner, Sharp’s description of “TANGO 176 nucleic acids which encodes PPCA which can be used to treat galactosialidosis[;] . . . methods for production of the disclosed proteins including using insect cells[;] . . . [and] pharmaceutical compositions of the disclosed nucleic acids and proteins” anticipates the claimed invention (Examiner’s Answer, pages 11-12).

Appellants concede that “Sharp does generically mention the production of proteins in insect cells when providing a [] list of the various forms of standard expression vectors and host cells that may be used to produce proteins” (Appeal Brief, page 13), but argue that “Sharp does not specifically teach the production of PPCA (i.e. TANGO 176) in insect cell culture for the purpose of making a pharmaceutical composition” (*id.*). In other words, appellants argue that the examiner has combined disparate parts of Sharp’s disclosure to arrive at a pharmaceutical composition comprising PPCA produced in insect cell culture and a pharmaceutically acceptable

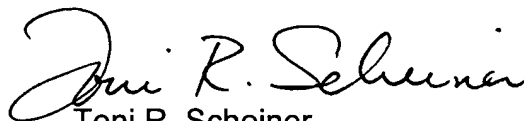
carrier. Appellants argue that “Sharp would not have conveyed to the skilled artisan the specific idea of producing PPCA in an insect cell for the purpose of producing a pharmaceutical composition” given “the state of the art at the time of the Sharp disclosure” as described in “the background section of [the present] application” (*id.*).

In our view, Sharp’s disclosure shares a similarity of subject matter with the claimed pharmaceutical compositions, but does not “clearly and unequivocally” describe them. Accordingly, the rejection of claims 8-13 as anticipated by Sharp is reversed.

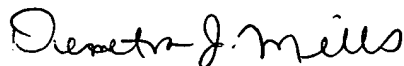
Summary

The rejections of claims 8-13 under 35 U.S.C. § 112, first paragraph, as lacking enablement and adequate written descriptive support are reversed. The rejection of claims 8-13 under 35 U.S.C. § 102(a) is reversed as well.

REVERSED



Toni R. Scheiner
Administrative Patent Judge



Demetra J. Mills
Administrative Patent Judge



Eric Grimes
Administrative Patent Judge

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